

WEST Search History

DATE: Thursday, May 12, 2005

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|--------------------------|---------------------------|--|----------------------------|
| | | <i>DB=USPT; PLUR=YES; OP=AND</i> | |
| <input type="checkbox"/> | L1 | heavychain or heavy-chain or hc or h-c or carboxyterminal or carboxylterminal or carboxy-terminal or carboxyl-terminal or (receptor near3 binding) or (targeting near3 moiety) or (receptor near3 domain) or (binding near3 moiety) or (receptor near3 moiety) or rbonthc or rbont-ch or bonthc or bont-hc | 54884 |
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| <input type="checkbox"/> | L3 | botulin or botulinum or botinolysin or botulism or botox or bttox or btn or btx or neurotoxin or neuro-toxin | 11128 |
| <input type="checkbox"/> | L4 | L3 and (l1 or l2) | 3434 |
| <input type="checkbox"/> | L5 | L4 and clostrid\$ | 1416 |
| <input type="checkbox"/> | L6 | (l1 or l2).clm. and l3.clm. | 31 |

END OF SEARCH HISTORY

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| (L1 or L2).clm. and L3.clm. | 31 |

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US-PAT-NO: 6713444

DOCUMENT-IDENTIFIER: US 6713444 B1

TITLE: Buforin I as a specific inhibitor and therapeutic agent for botulinum toxin B and tetanus neurotoxins

DATE-ISSUED: March 30, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|----------------------|------------|-------|----------|---------|
| Garcia; Gregory E. | Germantown | MD | | |
| Gordon; Richard K. | Potomac | MD | | |
| Moorad; Debbie R. | Rockville | MD | | |
| Doctor; Bhupendra P. | Potomac | MD | | |

ASSIGNEE-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY | TYPE CODE |
|--|---------------|-------|----------|---------|-----------|
| The United States of America as represented by the Secretary of the Army | Washington DC | | | | 06 |

APPL-NO: 09/ 570023 [PALM]

DATE FILED: May 12, 2000

PARENT-CASE:

CROSS REFERENCE TO RELATED APPLICATIONS This application is based on provisional application No. 60/134,216 filed May 14, 1999.

INT-CL: [07] A61 K 38/00, C07 K 14/00

US-CL-ISSUED: 514/2; 514/13, 514/21, 530/324, 530/326, 530/333, 530/344, 424/239.1, 424/9.1, 435/252.7

US-CL-CURRENT: 514/2; 424/239.1, 424/9.1, 435/252.7, 514/13, 514/21, 530/324, 530/326, 530/333, 530/344

FIELD-OF-SEARCH: 514/12, 514/13, 514/21, 530/324, 530/326, 530/333, 530/344, 424/239.1, 424/9.1, 435/252.7

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

| | | |
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| PAT-NO | ISSUE-DATE | PATENTEE-NAME | US-CL |
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| <input type="checkbox"/> <u>5936063</u> | August 1999 | Kim et al. | 530/324 |

☐ 6573244

June 2003

Gordon et al.

514/15

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ART-UNIT: 1653

PRIMARY-EXAMINER: Low; Christopher S. F.

ASSISTANT-EXAMINER: Kam; Chih-Min

ATTY-AGENT-FIRM: Arwine; Elizabeth

ABSTRACT:

The compounds of the invention are generally described by the formula:

X.sub.1 X.sub.2 B.sub.3 X.sub.4 B.sub.5 X*.sub.6 X.sub.7 X.sub.8

B.sub.9 X.sub.10 B.sub.11 X.sub.12 B.sub.13 X.sub.14

B.sub.15 X.sub.16 B.sub.17 X*.sub.18 X*.sub.19 B.sub.20

X.sub.21 X.sub.22 X.sub.23 Q.sub.24 F.sub.25 Z*.sub.26 X.sub.27

X.sub.28 B.sub.29 X.sub.30 B.sub.31 B.sub.32 X.sub.33 X.sub.34

B.sub.35 B.sub.36 X.sub.37 Z.sub.38 Z.sub.39 (1)

and the salts, esters, amides, and acyl forms thereof. Up to 15 amino acids may be truncated from the N-terminus and up to 6 amino acids may be truncated from the C-terminus. Each position represented by a letter indicates a single amino acid residue wherein B is a basic or polar/large amino acid or a modified form thereof; X is a small or hydrophobic amino acid or a modified form thereof; X* is a small or polar/large amino acid or a modified form thereof; Z is a polar/large or hydrophobic amino acid or a modified form thereof; Z* is Proline or a polar/large or hydrophobic amino acid or a modified form thereof. These compounds may be used to inhibit the protease activity of Botulinum B and tetanus toxins.

12 Claims, 10 Drawing figures

PGPUB-DOCUMENT-NUMBER: 20020068699
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020068699 A1

TITLE: Clostridial toxin derivatives and methods for treating pain

PUBLICATION-DATE: June 6, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|------------------|------------------|-------|---------|---------|
| Donovan, Stephen | Capistrano Beach | CA | US | |

ASSIGNEE-INFORMATION:

| NAME | CITY | STATE | COUNTRY | TYPE CODE |
|----------------------|--------|-------|---------|-----------|
| Allergan Sales, Inc. | Irvine | CA | US | 02 |

APPL-NO: 09/ 938112 [PALM]

DATE FILED: August 23, 2001

RELATED-US-APPL-DATA:

Application 09/938112 is a division-of US application 09/489667, filed January 19, 2000, PENDING

INT-CL: [07] A61 K 39/08, C07 K 14/33

US-CL-PUBLISHED: 514/12; 530/350

US-CL-CURRENT: 514/12; 530/350

ABSTRACT:

Agents for treating pain, methods for producing the agents and methods for treating pain by administration to a patient of a therapeutically effective amount of the agent. The agent can include a clostridial neurotoxin, or a component or fragment or derivative thereof, attached to a targeting moiety, wherein the targeting moiety is selected from a group consisting of transmission compounds which can be released from neurons upon the transmission of pain signals by the neurons, and compounds substantially similar to the transmission compounds.

DOCUMENT-IDENTIFIER: US 20040147716 A1

TITLE: Peptides comprising aromatic D-amino acids and methods of use

CLAIMS:

14. The method of claim 12, wherein the toxin is selected from the group consisting of botulinum toxins, ricin toxins, cholera toxins, and anthrax toxins or toxin subcomponents.

31. A method of reducing the ConA lectin binding to at least one of its receptors comprising delivering to the mammal a D-peptide comprising a pentapeptide core selected from the group consisting of Xaa.sub.1YYFF and Xaa.sub.1FYFF wherein Xaa.sub.1 is an amino acid of the D- or L-configuration independently selected from the group consisting of D, E, K, R, H, N, Q, C, S, T, G, A, V, L, I, M and P.

39. A method of reducing binding of TNFA to a TNFA receptor comprising delivering to the mammal a D-peptide comprising a pentapeptide core selected from the group consisting of FFFXaa.sub.1F, YFXaa.sub.1FF, YFYFXaa.sub.1, YWXaa.sub.1FF, WXaa.sub.1YXaa.sub.2F, WXaa.sub.1YFXaa.sub.2 and WXaa.sub.1FFXaa.sub.2 wherein Xaa.sub.1 and Xaa.sub.2 are amino acids of the D- or L-configuration independently selected from the group consisting of D, E, K, R, H, N, Q, C, S, T, G, A, V, L, I, M and P.

41. A method of reducing the binding of TGF.beta.1 to a TNF.beta.1 receptor comprising delivering to the mammal a D-peptide comprising a pentapeptide core selected from the group consisting of FFFXaa.sub.1W, FWFXaa.sub.1Xaa.sub.2, FYXaa.sub.1YF, FWXaa.sub.1Xaa.sub.2Xaa.sub.3, FXaa.sub.1YYW, FXaa.sub.1YYXaa.sub.2, FWXaa.sub.1WY, FFYWW, FXaa.sub.1Xaa.sub.2FXaa.sub.3, FYWXaa.sub.1Y, FYWXaa.sub.1W, FXaa.sub.1YFXaa.sub.2, FYYXXaa.sub.1, FWXaa.sub.1FF and FFXaa.sub.1WW wherein Xaa.sub.1, Xaa.sub.2 and Xaa.sub.3 are amino acids of the D- or L-configuration independently selected from the group consisting of D, E, K, R, H, N, Q, C, S, T, G, A, V, L, I, M and P.

PGPUB-DOCUMENT-NUMBER: 20040265935
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040265935 A1

TITLE: Botulinum toxin a peptides and methods of predicting and reducing immunoresistance to botulinum toxin therapy

PUBLICATION-DATE: December 30, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|--------------------|---------|-------|---------|---------|
| Atassi, M. Zouhair | Houston | TX | US | |

APPL-NO: 10/ 821669 [PALM]
DATE FILED: April 9, 2004

RELATED-US-APPL-DATA:

Application is a non-provisional-of-provisional application 60/462754, filed April 11, 2003,

INT-CL: [07] G01 N 33/554, G01 N 33/569

US-CL-PUBLISHED: 435/007.32
US-CL-CURRENT: 435/7.32

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

The present invention provides BoNT/A peptides as well as methods of predicting or determining immunoresistance to botulinum toxin therapy in an individual using BoNT/A peptides.

[0001] This application is based on, and claims the benefit of, U.S. Provisional Application No. 60/462,754, filed Apr. 11, 2003, and entitled Botulinum Toxin A Peptides And Methods Of Predicting And Reducing Immunoresistance To Botulinum Toxin Therapy, and which is incorporated herein by reference.

DOCUMENT-IDENTIFIER: US 20040265935 A1

TITLE: Botulinum toxin a peptides and methods of predicting and reducing immunoresistance to botulinum toxin therapy

CLAIMS:

1. A method of predicting or determining immunoresistance to botulinum toxin therapy in an individual, comprising determining the presence or absence in said individual of antibodies immunoreactive with two or more amino acid sequences selected from the group: 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1 [C10]; 1051-1069 of SEQ ID NO: 1 [C15]; 1121-1139 of SEQ ID NO: 1 [C20]; and 1275-1296 of SEQ ID NO: 1 [C31], or a conservative variant or immunoreactive fragment thereof, wherein the presence of antibodies immunoreactive with said two or more amino acid sequences indicates immunoresistance to botulinum toxin therapy.

17. The method of claim 1, 6 or 10, wherein said botulinum toxin therapy is BoNT/A therapy.

18. A method of preventing or reducing immunoresistance to botulinum toxin therapy in an individual, comprising administering to said individual a tolerogizing agent and two or more amino acid sequences selected from the group: 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1 [C10]; 1051-1069 of SEQ ID NO: 1 [C15]; 1121-1139 of SEQ ID NO: 1 [C20]; and 1275-1296 of SEQ ID NO: 1 [C31], or a conservative variant or an immunoreactive fragment thereof, thereby preventing or reducing immunoresistance to botulinum toxin therapy.

30. The method of claim 18, 22 or 26, wherein said botulinum toxin therapy is BoNT/A therapy.

31. A method of vaccinating an individual against botulinum toxin, comprising administering to said individual a vaccine comprising an adjuvant and two or more amino acid sequences selected from the group 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1 [C10]; 1051-1069 of SEQ ID NO: 1 [C15]; 1121-1139 of SEQ ID NO: 1 [C20]; and 1275-1296 of SEQ ID NO: 1 [C31], or a conservative variant or an immunoreactive fragment thereof, thereby producing an immune response to said botulinum toxin in said individual.

44. A method of removing botulinum toxin blocking antibodies from a patient, comprising the steps of (a) removing blood from a patient; (b) contacting said blood, or an antibody-containing component thereof with two or more amino acid sequences selected from the group 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1 [C10]; 1051-1069 of SEQ ID NO: 1 [C15]; 1121-1139 of SEQ ID NO: 1 [C20]; and 1275-1296 of SEQ ID NO: 1 [C31], or a conservative variant or an immunoreactive fragment thereof, under conditions suitable for forming a complex of each of said amino acid sequences and anti-botulinum toxin antibody; and (c) removing said complex from said blood or antibody-containing component thereof.

47. The method of claim 44, 45 or 46, comprising selectively removing IgG botulinum toxin blocking antibodies from said patient.

48. A method of predicting or determining immunoresistance to botulinum toxin therapy in an individual, comprising the steps of: (a) determining the level of IgG antibodies immunoreactive with said botulinum toxin in said individual; and (b) comparing said level of IgG antibodies to a control level of IgG antibodies, wherein an increase in said level of IgG antibodies in said individual as compared to said control level indicates immunoresistance to said botulinum toxin therapy.

51. The method of claim 48, wherein said control level of IgG antibodies is determined in an individual who has not been treated with botulinum toxin therapy.

52. The method of claim 48, wherein said control level of IgG antibodies is determined in an individual who is responsive to said botulinum toxin therapy.

53. The method of claim 48, wherein said botulinum toxin therapy is BoNT/A therapy.

54. A method of predicting or determining immunoresistance to botulinum toxin therapy in an individual, comprising determining the presence or absence in said individual of antibodies immunoreactive with a BoNT/A peptide having a length of at most 60 amino acids and comprising an amino acid sequence selected from the group:

7 445-471 of SEQ ID NO: 1, 487-513 of SEQ ID NO: 1, 515-541 of SEQ ID NO: 1, 529-555 of SEQ ID NO: 1, 543-569 of SEQ ID NO: 1, 557-583 of SEQ ID NO: 1, 585-611 of SEQ ID NO: 1, 599-625 of SEQ ID NO: 1, 655-681 of SEQ ID NO: 1, 669-695 of SEQ ID NO: 1, 683-709 of SEQ ID NO: 1, 711-737 of SEQ ID NO: 1, 739-765 of SEQ ID NO: 1, 767-793 of SEQ ID NO: 1, 781-807 of SEQ ID NO: 1, 809-835 of SEQ ID NO: 1, 823-849 of SEQ ID NO: 1, and 837-863 of SEQ ID NO: 1,

or a conservative variant or immunoreactive fragment thereof, wherein the presence of antibodies immunoreactive with said peptide indicates immunoresistance to botulinum toxin therapy, and with the proviso that said BoNT/A peptide is not SEQ ID NO:2.

66. The method of claim 64, wherein said Hc peptide comprises an amino acid sequence selected from the group:

10 amino acids 939-957 of SEQ ID NO: 1 amino acids 953-971 of SEQ ID NO: 1 amino acids 967-985 of SEQ ID NO: 1 amino acids 981-999 of SEQ ID NO: 1 amino acids 995-1013 of SEQ ID NO: 1 amino acids 1009-1027 of SEQ ID NO: 1 amino acids 1023-1041 of SEQ ID NO: 1 amino acids 1037-1055 of SEQ ID NO: 1 amino acids 1051-1069 of SEQ ID NO: 1 amino acids 1065-1083 of SEQ ID NO: 1 amino acids 1079-1097 of SEQ ID NO: 1 amino acids 1093-1111 of SEQ ID NO: 1 amino acids 1107-1125 of SEQ ID NO: 1 amino acids 1121-1139 of SEQ ID NO: 1 amino acids 1135-1153 of SEQ ID NO: 1 amino acids 1149-1167 of SEQ ID NO: 1 amino acids 1163-1181 of SEQ ID NO: 1 amino acids 1177-1195 of SEQ ID NO: 1 amino acids 1191-1209 of SEQ ID NO: 1 amino acids 1205-1223 of SEQ ID NO: 1 amino acids 1219-1237 of SEQ ID NO: 1 amino acids 1233-1251 of SEQ ID NO: 1 amino acids 1247-1265 of SEQ ID NO: 1 amino acids 1261-1279 of SEQ ID NO: 1, and amino acids 1275-1296 of SEQ ID NO: 1,

or an immunoreactive fragment thereof.

73. The method of claim 54, wherein said botulinum toxin therapy is BoNT/A therapy.

74. A method of preventing or reducing immunoresistance to botulinum toxin therapy in an individual, comprising administering to said individual a tolerogizing agent and a BoNT/A peptide, said peptide having a length of at most 60 amino acids and comprising an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof, thereby preventing or reducing immunoresistance to

botulinum toxin therapy, with the proviso that said BoNT/A peptide is not SEQ ID NO:2.

82. The method of claim 74, wherein said tolerogizing agent and BoNT/A peptide are administered prior to said individual receiving botulinum toxin therapy.

83. The method of claim 82, wherein said individual is at increased risk for immunoresistance to botulinum toxin therapy.

84. A method of vaccinating an individual against botulinum toxin, comprising administering to said individual a vaccine comprising an adjuvant and a BoNT/A peptide, said peptide having a length of at most 60 amino acids and comprising an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof, thereby producing an immune response to botulinum toxin in said individual, with the proviso that said BoNT/A peptide is not SEQ ID NO:2.